Complete Summary

GUIDELINE TITLE

Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 34 p. (Technology appraisal guidance; no. 118).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- September 26, 2006, Avastin (bevacizumab): Revisions to the WARNINGS and ADVERSE REACTIONS sections of the prescribing information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Metastatic colorectal cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Gastroenterology
Internal Medicine
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To assess the clinical effectiveness and cost-effectiveness of bevacizumab and cetuximab in the treatment of individuals with metastatic colorectal cancer (CRC)

More specifically, the objectives are:

- To evaluate the relative clinical effectiveness of bevacizumab and cetuximab in terms of progression-free survival, overall survival, tumour response rates, time to treatment failure and health-related quality of life (HRQoL) compared with current standard treatments
- To evaluate the adverse effect profiles of bevacizumab and cetuximab
- To estimate the incremental cost-effectiveness of bevacizumab and cetuximab compared with current standard therapies
- To estimate the annual cost to the National Health Service (NHS) in England and Wales

TARGET POPULATION

- The relevant population for the assessment of bevacizumab is people with untreated metastatic colorectal cancer (CRC).
- The relevant population for the assessment of cetuximab is people with epidermal growth factor receptor (EGFR)-expressing metastatic CRC who have previously failed on irinotecan-including therapy.

INTERVENTIONS AND PRACTICES CONSIDERED

1. First-line therapy using bevacizumab in combination with 5-fluorouracil plus folinic acid (5-FU/FA) or 5-FU/FA plus irinotecan
2. Second- or subsequent-line therapy using cetuximab in combination with irinotecan

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
  - Overall survival
  - Progression-free survival
  - Tumor response rates
  - Time to treatment failure
  - Adverse events/toxicity
  - Health-related quality of life
- Cost-effectiveness and cost-utility

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the School of Health and Related Research, the University of Sheffield (see the "Companion Documents" field).

Clinical Effectiveness

Search Strategy

The searches aimed to identify all literature relating to the clinical effectiveness and cost-effectiveness of bevacizumab and cetuximab in the treatment of metastatic colorectal cancer (CRC) (see Appendix 4 of the Assessment Report [see "Availability of Companion Documents" field). The main searches were conducted in April and May 2005. No language, study/publication, or date restrictions were applied to the main searches. Searches were performed in Medline, Embase, CINAHL, BIOSIS, the Cochrane Database of Systematic Reviews (CDSR), the Cochrane Controlled Trials Register (CCTR), the Science Citation Index and the National Health Services (NHS) Centre for Reviews and Dissemination databases (DARE, NHS, EED, HTA) and OHE HEED.

Inclusion and Exclusion Criteria

Phase III and Phase II randomised controlled trials (RCT) were included if they compared any of the proposed interventions with existing recommended comparators. Primary outcomes were identified as overall survival and/or progression-free survival. Secondary outcomes were identified as health-related quality of life, tumour response rates and adverse events. The use of data from Phase II studies and non-randomised studies was considered only where there was insufficient evidence from good quality Phase III trials, the former being studies appropriately powered to assess efficacy outcomes, rather than those directly associated with clinical effectiveness, and both being subject to selection bias.

For the assessment of bevacizumab, trials were included if they recruited participants with untreated metastatic CRC for first-line treatment with bevacizumab. Only trials which compared bevacizumab in combination with irinotecan and/or established fluorouracil-containing or releasing regimens given as first-line therapy were included in this review.

For the assessment of cetuximab, trials were included if they recruited participants with epidermal growth factor receptor (EGFR)-expressing metastatic CRC who had previously failed irinotecan-including therapy. The scope of this assessment was to compare treatment with cetuximab plus irinotecan as second- or subsequent-line therapy against oxaliplatin in combination with 5-fluorouracil/folinic acid (5-FU/FA) or active/best supportive care. It should be noted from the outset that no randomised or non-randomised studies of cetuximab met the inclusion criteria for this review. Therefore, all studies which included cetuximab as a second- or subsequent-line therapy for patients with metastatic CRC who were refractory to irinotecan were included in the review. The review of cetuximab is not a typical systematic review of clinical effectiveness, but rather represents a comprehensive and wide review of the current state of knowledge on the clinical effectiveness of cetuximab in the second- and subsequent-line treatment of patients with metastatic CRC.

Only trials which reported at least one of the primary outcomes, overall survival (OS) or progression-free survival (PFS) were included in the review. Survival duration was defined as the interval from randomisation to death. PFS was defined as the interval from randomization to disease progression or death during the study. Disease progression was defined according to the Response Evaluation Criteria in Solid Tumors (RECIST). For patients alive and without disease progression at the time of analysis, PFS was censored at the time of analysis. Secondary outcomes, tumour response rates, toxicities, and health-related quality of life, were extracted where reported. Tumour response rates were defined as the number of patients in each group who achieved a partial or complete response, however defined. Toxicities and quality of life data were abstracted as reported, however defined.

Cost-Effectiveness

Search Methods

Systematic literature searches were undertaken to identify all relevant studies relating to the cost-effectiveness of:

1. First-line treatment with bevacizumab in combination with 5-fluorouracil/folinic acid (5-FU/FA) or irinotecan plus 5-FU/FA as compared to 5-FU/FA or irinotecan plus 5-FU/FA in patients with metastatic CRC
2. Second- and subsequent-line treatment with cetuximab in combination with irinotecan in comparison to active/best supportive care or oxaliplatin plus 5-FU/FA in the treatment of patients with EGFR-expressing metastatic CRC who have previously failed on irinotecan-including cytotoxic therapy.

Medline search strategies for the cost-effectiveness review are presented in Appendix 4 of the Assessment Report (see "Availability of Companion Documents" field). Hand-searching of sponsor submissions to NICE was also undertaken in order to identify any further studies which were not identified by the electronic searches.

Studies Included in the Review of Cost-Effectiveness

The systematic searches did not identify any published studies relating to the cost-effectiveness of either bevacizumab or cetuximab in the treatment of metastatic CRC. The Roche submission to NICE included details of two mathematical models used to estimate the cost-effectiveness of bevacizumab in combination with irinotecan plus 5-FU/FA versus irinotecan plus 5-FU/FA alone, and bevacizumab in combination with 5-FU/FA versus 5-FU/FA alone. The Merck submission to NICE reported details of a mathematical model used to estimate the cost-effectiveness of second- and subsequent-line treatment using cetuximab plus irinotecan versus active/best supportive care. Appendix 5 of the Technology Assessment Report (see "Availability of Companion Documents" field) details the studies identified for inclusion in the review of cost-effectiveness.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Bevacizumab – The search retrieved seven citations for studies of bevacizumab as first-line therapy for people with metastatic colorectal cancer (CRC). Of the seven citations identified, three were randomised controlled trials (RCTs), one was a combined study of efficacy data from these three RCTs, and three were abstracts presented at the American Society of Clinical Oncology (ASCO) general meetings. Only the three RCTs identified were included in the assessment of clinical effectiveness. The combined analysis of efficacy data and the three additional abstracts were used to present a more complete overview of bevacizumab as first-line therapy for metastatic CRC.

Cetuximab – The search retrieved citations for studies of cetuximab as second- or subsequent-line therapy for people with metastatic CRC; however, none of these met the inclusion criteria for this systematic review. In addition, the manufacturer provided an addendum to their full submission outlining results from the MABEL trial.

Cost-Effectiveness

No published economic analyses of either bevacizumab or cetuximab were identified. The manufacturers of bevacizumab and cetuximab both submitted cost-effectiveness models, and the assessment group developed two models for each drug.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the School of Health and Related Research, the University of Sheffield (see the "Availability of Companion Documents" field.)

Clinical Effectiveness

Validity Assessment

Published papers were assessed according to the accepted hierarchy of evidence, whereby meta-analyses of randomised controlled trials (RCTs) are considered to be the most authoritative forms of evidence, and expert opinion is considered to be the least authoritative. Two researchers assessed papers, in order to give a narrative assessment of the potential for bias in the studies and, in the event that statistical synthesis (meta-analysis) was appropriate, to inform sensitivity analysis. A table summarising data on quality assessment can be found in Appendix 6 of the Assessment Report (see "Availability of Companion Documents" field).

Data Abstraction

All abstracts were read and those studies which met the inclusion criteria were identified. Data from identified studies, reviews and other evidence were extracted by the reviewer using a standardised data extraction form. The data extraction form used within this review is presented in Appendix 7 of the Assessment Report (see "Availability of Companion Documents" field).

Analysis

Results of eligible studies were to be statistically synthesised (meta-analysed) for trials with similar populations, interventions, and outcomes. However, meta-analysis was not undertaken within the systematic review of bevacizumab as the populations and control treatments used within the included trials differed. Owing to the paucity of evidence on the effectiveness of cetuximab in combination with irinotecan in the treatment of patients with epidermal growth factor receptor (EGFR)-expressing colorectal cancer (CRC) who are refractory to irinotecan, meta-analysis was not undertaken. It was stated prospectively, that sub-group analyses would be performed on the basis of whether 5-fluorouracyl/folinic acid (5-FU/FA) was delivered by bolus injection or continuous infusion. This is because it is widely believed that there is a systematic difference in treatment effect based on the mode of delivery which is likely to interact in different ways with the new interventions under evaluation.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical

experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

No published economic analyses of either bevacizumab or cetuximab were identified. The manufacturers of bevacizumab and cetuximab both submitted cost-effectiveness models, and the assessment group developed two models for each drug.

Bevacizumab – Manufacturer's Models

The manufacturer submitted two simple-state transition models with three health states: pre-progression, post-progression and death. Each model was based on data from a different bevacizumab study. The first was based on the study that compared bevacizumab plus irinotecan, fluorouracil, and leucovorin (IFL) with IFL, while the second was based on the larger of the two studies that compared bevacizumab plus 5-fluorouracil/leucovorin (5-FU/LV) with 5-FU/LV. In both models the analysis was carried out from the perspective of the National health Service (NHS). Data on progression-free survival for the treatment and control arms were taken from trial data, and an equal risk of death was applied following progression irrespective of treatment group. The models assumed equivalent utility scores for both the intervention and control groups, with a utility of 0.80 given to the pre-progression health state and 0.50 to the post-progression health state. Utility decrements associated with adverse events were not included. Pre-progression costs were calculated from the trials, augmented with data from other

published sources. For post-progression costs an assumption of 2000 pounds sterling a month was used, applied equally to both arms.

Bevacizumab – Assessment Group Models

The methods used for the models produced by the assessment group were similar to those used in the National Institute for Health and Clinical Excellence (NICE) appraisal of irinotecan, oxaliplatin and raltitrexed (NICE technology appraisal 93). The assessment group presented two models based on the same trials as used in the manufacturer's models. The models were simple-state transition models with costs and effects calculated from the perspective of the NHS. Unlike the manufacturer's models the outcome data were based on published overall survival curves from the two studies. The utility value for pre-progression was the same as was used in the manufacturer's models (0.80), whereas that for post-progression was slightly higher (0.60). Data on second-line and subsequent therapies were taken from a study that investigated the optimal sequence of oxaliplatin plus infusional 5-FU/FA (FOLFOX) and irinotecan plus 5-FU (FOLFIRI) as first- and second-line therapies, and were applied equally to treatment and control groups. Costs were calculated from study data and augmented from a range of sources including published literature and personal communications. Discounting was not used because the distribution of costs incurred over time was unknown and was not considered relevant by the assessment group because of the short time horizon in the model.

Cetuximab – Manufacturer's Model

The manufacturer's model for cetuximab used survival modelling to estimate the lifetime costs and benefits for patients receiving cetuximab combined with irinotecan compared with ASC/BSC. Two sets of analyses were presented. The first was based directly on survival data from the randomised controlled trial (RCT), whereas in the second analysis adjustments were made to the survival data to reflect a proposed continuation rule. Under the continuation rule patients would only continue to receive cetuximab beyond 6 weeks if there were either a partial or complete tumour response or an acne-like rash of grade 2 or above.

Cetuximab - Assessment Group Models

In the absence of direct comparisons of cetuximab plus irinotecan with active supportive care/best supportive care (ASC/BSC) or FOLFOX, the assessment group developed two models. The first was a threshold analysis considering the incremental benefit that cetuximab combined with irinotecan would have to provide over ASC/BSC in order to be considered cost effective. The second model was an indirect comparison of data from the arm receiving cetuximab and irinotecan in the RCT with data from other published studies of second-line ASC/BSC.

See section 4.2 in the original guideline document for detailed discussion of the manufacturer's and assessment group models.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- Bevacizumab in combination with 5-fluorouracil plus folinic acid, with or without irinotecan, is not recommended for the first-line treatment of metastatic colorectal cancer.
- Cetuximab in combination with irinotecan is not recommended for the second-line or subsequent treatment of metastatic colorectal cancer after the failure of an irinotecan containing chemotherapy regimen.
- People currently receiving bevacizumab or cetuximab should have the option to continue therapy until they and their consultants consider it appropriate to stop.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of bevacizumab and cetuximab for the treatment of metastatic colorectal cancer

POTENTIAL HARMS

Bevacizumab

The Summary of Product Characteristics (SPC) lists the following complications that may be associated with bevacizumab treatment: gastrointestinal perforation, wound-healing problems, hypertension, proteinuria, arterial thromboembolism, haemorrhage, and cardiomyopathy.

Cetuximab

One common side effect of cetuximab therapy is the development of an acne-like rash. The SPC notes that if a patient experiences a grade 3 or 4 skin reaction cetuximab treatment must be interrupted, with treatment being resumed only if the reaction resolves to grade 2. In addition, the SPC lists infusion-related reactions and respiratory disorders that may be associated with treatment with cetuximab.

For full details of side effects, see the SPC available at http://emc.medicines.org.uk/.

CONTRAINDICATIONS

CONTRAINDICATIONS

Bevacizumab is contraindicated in patients who are pregnant, have untreated central nervous system metastases, have hypersensitivity to the active substance or to any of the excipients, or have hypersensitivity to products derived from Chinese hamster ovary cell cultures or other recombinant human or humanised antibodies.

For full details of contraindications, see the Summary of Product Characteristics (SPC), available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation

- The Healthcare Commission assesses the performance of National Health Services (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on NICE website (www.nice.org.uk/TA114) (see also "Availability of Companion Documents" field).
    - Audit criteria to monitor local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. London (UK):

National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 34 p. (Technology appraisal guidance; no. 118).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jan

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 2 p. (Technology appraisal 118). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Costing statement: bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 1 p. (Technology appraisal 118). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Bevacizumab and cetuximab for metastatic colorectal cancer. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 9 p. (Technology appraisal 118). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- The use of bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. Assessment report. School of Health and Related Research (ScHARR), The University of Sheffield. 2006 Feb. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1199. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. Understanding NICE guidance – Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jan. 4 p. (Technology appraisal 118).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1200. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on June 26, 2007.

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